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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/538,927	06/13/2005	Hisayoshi Fujiwara	FUJIWARA3	5998

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EXAMINER	
XIE, XIAOZHEN	

ART UNIT	PAPER NUMBER
1646	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/538,927	FUJIWARA ET AL.	
	Examiner	Art Unit	
	Xiaozhen Xie	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 April 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5 and 8-11* is/are pending in the application.

4a) Of the above claim(s) *8* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5 and 9-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *13 June 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *20060911, 20070105*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments, And/Or Claims

The Information Disclosure Statements (IDS) filed 11 September 2006 and 5 January 2007 have been entered.

Election/Restrictions

Applicant's election with traverse of Group I, claims 1-5 and 9-11, in the response received 23 April 2007, is acknowledged.

Applicant argues that Morgan et al. describe "using Filgrastim (granulocyte colony-stimulating factor) for hematological support" (Abstract, and pp. 2393, right column). Applicant argues that the G-CSF is used for the treatment of granulocytopenia, but is not used for the treatment of cardiac disease. Applicant argues that since the Morgan citation does not destroy unity of invention, Group II (claim 8) should be examined along with Group I. Applicant further argues that even the requirement is correct, it would not constitute a serious burden to examine both groups, since no separate classification has been demonstrated.

Applicant's arguments have been fully considered but have not been found to be persuasive.

Morgan et al. teach that the primary limitation of cancer chemotherapeutic drugs, doxorunicin and related anthracyclines, has been dose-dependent cardiac toxicity, which can result in a congestive cardiomyopathy due to myocyte loss (pp. 2343, right column, 2nd paragraph in Discussion). The purpose of Morgan et al.'s study is to reduce

myocardial toxicity by using G-CSF for hematological support, e.g., through increasing WBC numbers (treating granulocytopenia), which leads to the treatment of congestive cardiomyopathy. Since the 1st claimed invention has no special technical feature, it cannot share a special technical feature with the other claimed inventions. Therefore, there is no single general inventive concept, and unity of invention is lacking. Further, the PCT rules do not provide for the examination of multiple inventions in one application.

The requirement is still deemed proper and is therefore made FINAL. Claims 6 and 7 are cancelled. Claims 1-5 and 8-11 are pending. Claim 8 is withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Claims 1-5 and 9-11 are under examination.

Information Disclosure Statement

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for treating non-ischemic heart failure comprising administering to a patient in need thereof a granulocyte colony-stimulating factor (G-CSF), does not reasonably provide enablement for any colony-stimulating factor (CSF). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in *In re* Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill, the level of predictability in the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention based on the content of the disclosure. See also *Ex parte* Forman, 230 USPQ 546 (BPAI 1986).

The claims are broad in that they encompass the use of any CSF for treating non-ischemic heart failure. The specification discloses that the long-term administration

of G-CSF ameliorates progressive myocardial fibrosis, left ventricular remodeling and heart failure in an animal model of cardiomyopathy (pp. 2, line 25 through pp. 3, line 1). The specification, however, does not provide guidance for using any CSF to treat non-ischemic heart failure. Bath et al. (Cochrane Database Syst. Rev., 2007, Apr. 18; (2):CD005207) teach that CSFs, also called haematopoietic growth factors, regulate bone marrow production of circulating red and white cells, and platelets. CSFs include stem cell factor (SCF), erythropoietin (EPO), granulocyte colony stimulating factor (G-CSF), granulocyte-macrophage colony stimulating factor (GM-CSF), macrophage-colony stimulating factor (M-CSF, CSF-1), and thrombopoietin (TPO), or analogues of these. The effect of different CSFs on haematology measures in patients with stroke varies (see Abstract). Also, Dempke et al. (Anticancer Res., 2000, 20(6D):5155-5164) teach that EPO, G-CSF and GM-CSF are currently licensed for use in cancer patients and play a significant role in the management of anemia and neutropenia following myeloblative chemotherapy. Although thrombopoietin (TPO) has been found to induce megakaryocyte differentiation *in vitro*, it is unlikely to enter routine clinical use for treatment of post-chemotherapy thrombocytopenia, since results of clinical trials are not very encouraging, mainly because TPO is difficult to schedule and platelet aggregation may occur (see Abstract). Therefore, different CSFs have different activities/functions, and not all of them can be used clinically for therapeutic uses. The specification does not teach what other CSFs can provide the same therapeutic use for treating non-ischemic heart failure as G-CSF. One of skill in the art would not know how to use other

agents. Thus, undue experimentation would be required for the artisan to practice the invention as broadly claimed.

Due to the large quantity of experimentation necessary to determine whether any CSF can be used for treating non-ischemic heart failure, the lack of direction/guidance presented in the specification, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes that CSFs mediate different biological activities, and not all CSFs can be used *in vivo* as a therapeutic drug, and the breadth of the claims which encompass any CSFs, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5 and 9-11 are rejected under 35 U.S.C. 102(b) as being anticipated by Cohen et al (WO 98/27995).

Claims 1-5 and 9-11 are drawn to a method for treating non-ischemic heart failure comprising administering to a patient in need thereof a colony-stimulating factor (CSF) as an active ingredient in an amount effective for treating non-ischemic heart failure (claim 1), wherein the non-ischemic heart failure is caused by exacerbation of cardiomyopathy, and the cardiomyopathy is idiopathic cardiomyopathy and dilated

cardiomyopathy (claims 2-4), wherein the CSF is granulocyte colony-stimulating factor (G-CSF) (claims 5, 9-11).

WO 98/27995 teaches a method of treatment of mammalian subjects at risk of, afflicted with, loss of, or damage to myocardium, and the subjects include patients who suffered a physical trauma to the heart (e.g., in an automobile accident), patients diagnosed with congestive heart failure, or patients with chronically deteriorating myocardium (e.g., due to congestive heart failure or chronic myopathy) (pp. 5, lines 11-17; pp. 11, lines 4-13; pp. 19, lines 19-22). "Congestive heart failure (CHF)" is generally considered equivalent to a dilated cardiomyopathy (see Feldman, US 6,221,851 B1, column, 1, lines 17-54). The method of WO 98/27995 comprises implanting myogenic precursor cells into the subject, and treating the subject subsequent to implantation with pharmaceutical compositions comprising morphogens, in combination with G-CSF, through systemic routes of administration (in particular, intravenous and intraperitoneal) (pp. 5, lines 19-21; pp. 10, lines 7-20). Therefore, WO 98/27995 anticipates the instant claims.

Claims 1-5 and 9-11 are rejected under 35 U.S.C. 102(b) as being anticipated by Morgan et al. (Clin. Cancer Res., 1997, 3:2337-2345, reference provided in the previous office action).

Claims 1-5 and 9-11 are drawn to a method for treating non-ischemic heart failure comprising administering to a patient in need thereof a colony-stimulating factor (CSF) as an active ingredient in an amount effective for treating non-ischemic heart

failure (claim 1), wherein the non-ischemic heart failure is caused by exacerbation of cardiomyopathy, and the cardiomyopathy is idiopathic cardiomyopathy and dilated cardiomyopathy (claims 2-4), wherein the CSF is granulocyte colony-stimulating factor (G-CSF) (claims 5, 9-11).

Morgan et al. teach a method of treating metastatic breast cancer with high dose chemotherapy and G-CSF for hematological support. Morgan et al. teach that the primary limitation of cancer chemotherapeutic drugs, doxorunicin and related anthracyclines, has been dose-dependent cardiac toxicity, which can result in a congestive cardiomyopathy due to myocyte loss (pp. 2343, right column, 2nd paragraph in Discussion). Morgan et al. teach that treatment with two cycles of high-dose cyclophosphamide and doxorubicin, using G-CSF for hematological support, is safe and has demonstrated therapeutic activity in patients who have previously received ≤ 150 mg/m^2 anthracycline (pp. 2344, right column, last paragraph in Discussion). Therefore, Morgan et al. anticipate the instant claims.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re

Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 2, 5 and 9 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 17 of copending Application No: 10/924,197.

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim not is patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

Here, Claims 1 and 17 of the '197 application are drawn to a method for treating heart diseases and vascular diseases (e.g., heart failure, cardiac myopathy), comprising administering a polypeptide having G-CSF activity under bone marrow suppressed

conditions. The method of the '197 application differs from the method claimed in the instant application in that the instant application is directed to treating non-ischemic heart failure, which is caused by exacerbation of cardiomyopathy, comprising administering a CSF, and wherein the administration in the '197 application is under bone marrow suppressed conditions. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are broader in scope, encompassing a genus of CSF molecules and disease conditions related to the species claimed in the '197 application. That is, claims 1, 2, 5 and 9 are anticipated by claims 1 and 17 of the '197 application.

Conclusion

NO CLAIM IS ALLOWED.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Xiaozhen Xie, Ph.D whose telephone number is 571-272-5569. The examiner can normally be reached on M-F, 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary B. Nickol, Ph.D. can be reached on 571-272-0835. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Xiaozhen Xie, Ph. D.
July 2, 2007

Eileen B. O'Hara

EILEEN B. O'HARA
PRIMARY EXAMINER